UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,364	08/24/2001	Vincent J . Wacher	AUMX-008/02US	3874

23419 7590 02/12/2003

COOLEY GODWARD, LLP
3000 EL CAMINO REAL
5 PALO ALTO SQUARE
PALO ALTO, CA 94306

EXAMINER
KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,364	WACHER ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,32-36,38-40,43,52-55,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,32-36,38-40,43,52-55,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Summary of Action

I. Applicant's arguments with respect to claims 23, 32-36,38-40, 43 and 52-55 have been considered but are moot in view of the new ground(s) of rejection.

II. The rejection of claim 43 and 52-54 under 35 USC 112, second paragraph paragraph, will not be maintained in light of the amendment.

III. The rejection of claims 23, 32-36, 38-40, 43 and 52-55 under the 35 USC 102(b) as being anticipated by Cheng et al. will not be maintained in light of Remarks.

IV. The rejection of claim 55 under 35 USC 112, second paragraph, will be maintained for the reason of the record.

V. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 USC 112, first paragraph.

VI. Claims 23, 32, 34-36, 38-40, 43, 52 and 54-55 are rejected under the 35 USC 102(b) as being anticipated by Salatinjants (US 4716173).

VII. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimamura et al (US 5807564 A)

VIII Claims 23, 36, 38, 40, 43, 52-55 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Xiong et al. (US 6299925 B1)

Status of Application

1. By amendment filed October 30, 200, 2002, Claim 43 have been amended and Claims 58 and 59 have been newly added.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the prior application, US Application No. 09/264,215) upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 23, 32-36, 38-50, 43, 52-55 and 58-59 of this application. The prior application provide insufficient direction or guidance in using (-)-epicatechin gallate, (-)-epigallocatechin gallate, (-)-gallocatechin gallate and tannic acid for formulating or reformulating an oral pharmaceutical composition. Therefore, applicants cannot obtain the benefit of earlier filing date of the prior application in regards to the newly disclosed information in this application. ***Information Disclosure Statement***

3. The information disclosure statement filed February 25, 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

4. Acknowledgment is made of applicants filing of ATTACHMENTS FOR RESPONSE MAILED OCTOBER 30, 2002. Applicants have submitted with three references-Ensminger, A.H. et al., Foods and Nutrition Encyclopedia, 2nd ed., 1:100 (1994); Stuckey, B.N., "Antioxidants as Food Stabilizers" CRC Handbook of Food Additives, 2nd ed., pp. 185-196(1980); and 21 C.F.R. 170.3(o)(3), 4-1-98 edition. If applicants desire to have the examiner

consider those references, applicants should submit in information disclosure statement (PTO 1449). It has been placed in the application file, but the information referred to therein has not been considered.

Election/Restriction

5. Acknowledgment is made of applicants election of Group II invention, claims 23, 32-36, 38-40 and 52-55. Applicants request for including the product claims, claims 41-42 and 57, along with the elected Group II invention is not considered persuasive. Since the instant invention is subjected to PCT Rule (rather than US Restriction requirement), the restriction between distinctive inventions, Group I-III, which are not so linked by the same or a corresponding special technical feature as to from a single general inventive concept deems proper and made Final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for a method of formulating or reformulating a drug which is subject to CYP3A biotransformation, does not reasonably provide enablement for the term "reformulating an existing oral pharmaceutical composition". The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification discloses that gallic acid esters (e.g., epicatechin gallate, epigallocatechin gallate, gallocatechin gallate and tannic acid) are useful in a method to increase the bioavilability of orally administered pharmaceutical compounds. The present invention is based on the activity of the claimed gallic acid esters (e.g., epicatechin gallate, epigallocatechin gallate, gallocatechin gallate and tannic acid) in inhibiting drug cytochromes P450 biotransformation, more specifically CYP3A, in the gut to increase drug bioavailability. The specification provides enabling disclosures for the gallic acid esters in inhibiting metabolism of drugs that undergo significant cytochrome P450 metabolism. Furthermore, the specification provides enabling disclosures for formulating or reformulating a drug that undergoes significant cytochrome P450 3A enzyme metabolism by adding sufficient amount of said gallic acid ester to the drug such that systemic absorption of the drug would be increased. However, the instant specification fails to provide adequate direction or guidance regarding whether said gallic acid ester can be practiced with other drugs that are not subject to P450 CYP3A metabolism. The specification fails to provide sufficient information regarding how to formulate non-P450 CYP3A biotransformation drug with said gallic acid ester. The breadth of the instant claims includes not only drugs that undergoes P450 CYP3A metabolism, but also non-P450 CYP3A biotransformation drug. The specification disclosure is insufficient to enable one skilled in the art to practice the invention without undue amount of experimentation. Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue

experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors:

1) the quality of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working example,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

Furthermore, applicants fail to provide information allowing the skilled artisan to ascertain "a pharmaceutical compound", "an existing composition" or "an existing oral pharmaceutical composition" without undue experimentation. The instant claims read on any pharmaceutical compounds or composition, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 55 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 55 is not clear at all which components should be present in the reformulated oral composition, which generously described as "containing less than all components present in the existing pharmaceutical composition plus the gallic acid ester".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 23, 32, 34-36, 38-40, 43, 52 and 54-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Salatinjants (US 4716173).

Salatinjants teaches an oral composition adapted to prolong the residence time of drugs in the circulating plasma prepared by admixing drugs (e.g., sulfa, cinchona alkaloid drugs) with other prolongating components including tannic acid (col. 1, lines 42-44 and 53-61; compositions of Drug No. 1 and 2; Table I; column 3, line 59 thru column 4, line 17; col. 4, lines 19-36; claims 1-3). Prolonging the residence time of a drug in the circulating plasma leads to a higher bioavailability of the drug at its target.

Although the prior art references are silent about "the gallic acid ester is present in an amount sufficient to produce a concentration of the gallic acid ester in the lumen of the gut of the mammal of at least 0.1 times a Ki or apparent Ki of CYP3A inhibition of the compound" in

claim 34; "at least 10% of the difference between bioavailability in the absence of the gallic acid ester and complete oral bioavailiability" in claim 35; "the gallic acid ester is covalently bound to the pharmaceutical compound in claim 39; and the functional property of "gallic acid ester" as "a counter ion of the pharmaceutical compound" in claim 38, the referenced gallic acid ester (e.g., epigallocatechin gallate) in the claimed range concentration in said composition must inherently possess those properties or characteristics. Therefore, the reference clearly anticipates the claimed invention.

9. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimamura et al. (US 5807564 A).

Shimamura discloses an improved antibiotic composition prepared by admixing 20-120 μg/ml catechin, preferably (-)epicatechin gallate, (-)epigallocatechin gallate, with 2-35 μg/ml antibiotic (e.g., oxacillin, methicillin, aminobenzyl penicillin, tetracycline, choramphenicol, cephalexin, penicillin G and amikacin), see column 3, lines 43-49; column 5, lines 41-44; Examples; Claims). The reference teaches that said composition is prepared in oral form (column 5, lines 42-47).

It is indicated in the present specification that many of the gallic acid used in the practice of the present invention are commercially available compounds or may be readily synthesized by methods that are well known in the art (page 4, lines 25-27). However, there is no indication in present claims that said gallic acid, namely (-)epicatechin gallate, (-)epigallocatechin gallate, (-)gallocatechin gallate or tannic acid, must essentially be used in the isolated form. Thus, claims seem to include methods wherein epicatechin gallate, epigallocatechin gallate, gallocatechin

gallate or tannic acid are admixed with a pharmaceutical compound in the form of tea extract. Thus, The reference anticipates the claimed invention.

Although the prior art references are silent about "the gallic acid ester is present in an amount sufficient to produce a concentration of the gallic acid ester in the lumen of the gut of the mammal of at least 0.1 times a Ki or apparent Ki of CYP3A inhibition of the compound" in claim 34; "at least 10% of the difference between bioavailability in the absence of the gallic acid ester and complete oral bioavailiability" in claim 35; "the gallic acid ester is covalently bound to the pharmaceutical compound in claim 39; and the functional property of "gallic acid ester" as "a counter ion of the pharmaceutical compound" in claim 38, the referenced gallic acid ester (e.g., epigallocatechin gallate) in the claimed range concentration in said composition must inherently possess those properties or characteristics. Therefore, the reference clearly anticipates the claimed invention.

10. Claims 23, 36, 38, 40, 43, 52-55 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Xiong et al. (US 6299925 B1).

Xiong teaches the claimed method of formulating an effervescent green tea extract formulation prepared by admixing a concentrated green tea plant extract having (-)epigallocatechin gallate with vitamins, ionic minerals and Herb/botanical extract (Examples, Claims 1, 6, 13. 14., 17-18).

It is indicated in the present specification that many of the gallic acid used in the practice of the present invention are commercially available compounds or may be readily synthesized by methods that are well known in the art (page 4, lines 25-27). However, there is no indication in present claims that said gallic acid, namely (-)epicatechin gallate, (-)epigallocatechin gallate,

(-)gallocatechin gallate or tannic acid, must essentially be used in the isolated form. Thus, claims seem to include methods wherein epicatechin gallate, epigallocatechin gallate, gallocatechin gallate or tannic acid are admixed with a pharmaceutical compound in the form of tea extract. Thus, The reference anticipates the claimed invention.

Although the prior art references are silent about the functional property of "gallic acid ester" as "a counter ion of the pharmaceutical compound" in claim 38, such characteristic or property is deemed to be inherent to the composition. Therefore, the reference clearly anticipates the claimed invention.

Conclusion

11. No Claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600